UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,490	09/24/2003	Gilbert R. Gonzales	GONZ-07	3979

26875 7590 04/30/2008

WOOD, HERRON & EVANS, LLP
2700 CAREW TOWER
441 VINE STREET
CINCINNATI, OH 45202

EXAMINER	
HOLT, ANDRIAE M	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
04/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,490	GONZALES ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Andriae M. Holt.

Claims 1-4 and 6-22 are pending in the application.

Status of the Claims

The rejection of claims 1-4 and 6-22 rejected under 35 U.S.C. 103(a) as being unpatentable over Ackman et al. in view of Zhang et al. **is withdrawn** in view of applicants amendment and response. However, the rejection will be reinstated upon cancellation of new matter.

The rejection of claims 1-4 and 6-22 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn** in view of applicant's amendment and response.

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new matter introduced, "avoid a sedative

effect", lacks written description as originally filed. While the specification does provide for the treatment of a sedative effect, it does not state "avoid". In the broadest since of the term avoid as defined by Merriam-Webster, is to prevent the occurrence or effectiveness of or refrain from, wherein, treat is to act upon with some agent to improve or alter.

Claim 1-4, 8,-12 and 16-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a pharmaceutical composition comprising an analgesic dosage formulation effective to treat acute pain and avoid a sedative effect with the dosage formulation including an oral dissolution agent, a buffer and methadone. In view of University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886, (U.S. Court of Appeals Federal Circuit, 2004), the claims do not identify what the effective amount to treat acute pain and avoid a sedative effect would be. At best, it simply indicates that one should run tests using a varied amount of dose ranges in the hope that at least one of the many dose ranges will provide the analgesic dosage to treat the acute pain without causing sedation. The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art,* (2) *partial structure,* (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention.*

While all of the factors have been considered, only those required for a *prima facie* case are set forth below.

The specification discusses on page 10, lines 18-25, that generally the composition comprises methadone in a dosage of at least about 0.5 mg and that in one embodiment the composition comprises methadone in a dosage range from about 2 mg to about 50 mg and in another embodiment an amount ranging from about 2 mg to about 10 mg per dose for the treatment of acute pain, however it does not disclose what the effective dosage range would be to treat acute pain and additionally avoid a sedative effect. The specification also discloses that the precise amount of methadone generally depends upon many factors, such as age, size, weight, gender and medical history of the targeted patient population again for the treatment of acute pain.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claims indicates that these claims are drawn to any dosage amount that may be effective to treat acute pain without causing sedation. There are only a few dosage ranges explicitly disclosed, see claims 6-7, 13-14 and 21-22. The specification discloses specific dosage ranges in the example on page 23, lines 16-17, 3.5 mg to about 4 mg, and lines 18-20, 5 mg, 10 mg, up to about 40 mg to treat pain, not directed to the fact that these amounts will also avoid a sedative effect.

The disclosure of the disclosed dosage ranges may provide an adequate written description of an effective dosage range in treating pain, when the dose ranges disclosed is representative of the effective dosage range, but it does not provide adequate written description for the effective amounts that would not cause sedation. The present claims encompass any and all effective dosage formulations that can be used to treat acute pain without causing sedation. However, Applicant does not provide any guidance as to what the maximum or minimum dosage amounts could be administered that would be able to treat pain and additionally avoid a sedative effect. There is substantial variability among the dosage ranges encompassed within the scope of the claims because the specific dosage ranges disclosed on page 10 of the specification and in the example on page 23 are only representative dosage ranges amongst a wide range of formulation dosages of methadone that can have widely differing effects and corresponding biological activities.

Weighing all the factors, the breadth of the claims reading on compositions yet to be discovered, the lack of correlation between structure and function of the compositions, level of knowledge and skill in the art, one of ordinary skill in the art would not recognize from the disclosure that the applicant was in possession of an analgesic dosage formulation effective to treat acute pain without causing sedation. At best, it simply indicates that one should run tests using a varied amount of dose ranges in the hope that at least one of the many dose ranges will provide the analgesic dosage to treat the acute pain without causing sedation. The specification does not provide a representative number of dosage ranges to describe the claimed dosage ranges. In

essence, the specification simply directs those skilled in the art to go figure out for themselves the effective amount of an analgesic dosage formulation to give to treat acute pain without causing sedation.

The written description requirement is not satisfied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-11, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Shaw et al. (3,980,766).

Shaw et al. disclose drugs that are suitable for therapy in treatment of narcotic drug addiction for oral use such as methadone (methadone, instant invention) that are formulated to prevent injection abuse through concentration of the active component in aqueous solution by incorporating in a solid dosage or tablet form (Abstract). Shaw et al. disclose in forming compositions and tablets one or more additives are incorporated which have the effect of deterring concentration by causing a rapid increase in viscosity during evaporation of an aqueous solution of the composition. Shaw et al. disclose that for this purpose various ingestible solids having thickening capability can be employed including lactose, sucrose, mannitol, sorbitol, starches, microcrystalline cellulose, sodium carboxymethyl cellulose, methylcellulose, ethyl cellulose, gum acacia (col. 2,

lines 5-20)(specific oral dissolution agents, instant invention). Shaw et al. disclose that separate investigation into the solubility of methadone in the general pH range of 6 to 9 was conducted. Shaw et al. further disclose that it appears that at a pH of 7 or lower, an aqueous solution of sufficient strength for injection to achieve a "high" can be prepared, but above pH 7 it becomes increasingly difficult to prepare a solution of sufficient strength and at a pH of 7.50 the solubility of methadone becomes so low as to completely frustrate its improper use by injection (col. 2, lines 33-68). Shaw et al. disclose the reduced solubility may be attained either by a composition which produces a pH of about 7.5 to 10 directly upon dispersion in water, or by a composition which upon initial dispersion produces a pH of at least 6 (pH 6, instant invention) which then increased to pH 7.5 or more upon concentration (col. 3, lines 1-6)(pH range 7 to about 10, instant invention). Shaw et al. disclose that typical ingestible solids which provide an alkaline pH in aqueous solution include soluble alkali metal and alkaline earth metal carbonates, bicarbonates, phosphates and acid phosphates (col. 3, lines 9-13) (specific buffers, instant invention).

Shaw et al. disclose in col. 4, example 1, lines 21-68, a 40 mg formulation of methadone, including methadone (methadone, instant invention), mannitol, lactose, and corn starch (dissolution agent, instant invention) and sodium bicarbonate (buffer, instant invention). Shaw et al. disclose that tablets containing from 5 to about 100 mg of methadone HCL can be formed from the identical composition according to therapeutic use (dose ranges, instant invention). In reference to the intended use of the formulation to treat acute pain and avoid sedative effect, through the oral mucosa, the compounds

and formulations of Shaw et al. are the same as Applicant's compounds and formulations. The treatment through the oral mucosa is intended use without imparting structural limitations. Shaw et al. discloses tablet formulations that are capable of performing the intended use. Thus, the skilled artisan would recognize that the compounds and formulations are inseparable from its properties. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990), "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." Hence, all the properties associated with Applicant's compounds and formulations would also be possessed by the compounds and formulations of Shaw et al. In reference to the absorption of the methadone through the oral mucosa, it is noted that Shaw et al. meet all the limitations of the claims.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Coleman et al. (2002/0106407).

Coleman et al. disclose methods and formulations for treating breakthrough pain (page 2, paragraph 18). Coleman et al. disclose that the first step of the method is to deliver the analgesic to the patient's blood stream by a noninvasive delivery technique. Coleman et al. further disclose the noninvasive delivery includes transdermal and transmucosal delivery and any other delivery routes that do not involve the puncture or incision of a patient's skin (page 3, paragraph 20). Coleman et al. disclose on page 9-10, claims 19-21, 24 and 28-29, a drug formulation comprising a drug and a carrier for administering the drug which provides the user control over rate of absorption to

maintain optimal pharmacokinetic profile, and optimal pharmacodynamic profile. Coleman et al. further disclose the drug is selected from methadone (methadone, instant invention) that is delivered transmucosally. Coleman et al. disclose the carrier comprises a combination of pharmaceutical ingredients. Coleman et al. disclose the dosage form is a lozenge (lozenge, instant invention) and a lozenge attached to a handle (lollipop, instant invention). Coleman et al. meet all the limitations of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 6-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw et al. (3,980,766) in view of Coleman et al. (2002/0106407).

Applicant's invention

Applicant claims a pharmaceutical composition comprised of an oral dissolution agent, a buffer and methadone that can be used to treat acute pain and avoid a sedative effect. Applicant claims the composition is a solid formulation selected from a lozenge or a lollipop.

Determination of the scope of the content of the prior art (MPEP 2141.01)

The teachings of Shaw et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Difference between the prior art and the claims (MPEP 2141.02)

Shaw et al. do not teach the specific solid formulations of claims 4, 12 and 16, lozenge or lollipop. It is for this reason Coleman et al. is joined.

The teachings of Coleman et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Finding of obviousness/Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the two cited references to make a solid methadone formulation in the form of a lozenge or a lollipop. Shaw et al. teach it is within the skill of one skilled in the art to make a solid methadone formulation, oral dissolution agents and alkaline buffers that have increased viscosity and reduced

solubility. Coleman et al. teaches it is within the skill of one skilled in the art to make a methadone drug formulation that is delivered transmucosally in the form of a lozenge or a lozenge attached to a handle to treat breakthrough pain and reduces the likelihood that a patient will suffer unacceptable adverse side effects. Thus, one would have been motivated to make this combination in order to receive the expected benefit of lozenge or lollipop formulation of methadone that can deliver an analgesic to a patient's bloodstream noninvasively and that during storage is stable, but upon dissolution in the oral cavity has a high dissolution rate and solubility. Given the state of the art as evidenced by the teachings of the cited references, and absent any evidence to the contrary, there would have been a reasonable expectation of success in combining the teachings of the cited references to produce an effective solid analgesic formulation that provides noninvasive therapy with the reduction of unwanted side effects.

None of the claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/Sharmila Gollamudi Landau/
Primary Examiner, Art Unit 1611